

Anaphylactoid Reactions due to Pancuronium

Junken KOH, Ryo SUMITA, Mayumi TAKASAKI and Yoshihiro KOSAKA

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Pancuronium bromide is a widely used muscle relaxant having little side-effect on cardiovascular system and inducing no or little release of histamine. However, six cases of anaphylactoid reactions due to histamine release has been reported. This paper presents a recently encountered case of anaphylactoid reactions to pancuronium bromide with clinical symptoms of cardiovascular collapse and generalized skin flushing.

Case Report

A 65-year-old man, 163 cm in height and 56 kg in weight, was scheduled for an esophageal reconstruction under the diagnosis of esophageal cancer. He had a history of rib fracture six years ago but had no other serious disease and no history of asthma or drug allergy.

Physical and laboratory examinations revealed his conditions within normal limits with the exception of relatively mild proteinemia (6.5 g/dl).

He was premedicated with 0.5 mg of atropine sulfate and 50 mg of hydroxyzine intramuscularly one hour prior to anesthesia. On arrival in the operating room, he was sedate and cooperative. Anesthesia was induced with 375 of thiamylal intravenously. After the administration of 60 mg of SCC, a Carlens' double-lumen tracheal tube was inserted for differential lung ventilation during operation. Anesthesia was maintained with fentanyl, and nitrous oxide (4 l)

and oxygen (2 l) under controlled ventilation. An Angiocath 22-gauge catheter was cannulated into the left radial artery for monitoring the blood pressure.

Ten minutes after induction of anesthesia, 4 mg of pancuronium were administered, while attempting insertion of a Swan-Ganz thermodilution catheter through the right internal jugular vein. As a bucking of the patient was recognized a few minutes later, further 2 mg of pancuronium were administered. After a little while, sudden hypotension appeared, simultaneously causing a drop of blood pressure from 120/80 mmHg to 42/20 mmHg and a heart rate increase from 70 to 140 beats/min. On accomplishing Swan-Ganz catheterization, the patient developed general skin flushing over the entire body. Bronchial spasm was suspected, but auscultation over the both lungs disclosed no wheezing, and the peak inspiratory pressure did not increase. The arterial blood gas parameters were pH 7.327, Pco₂ 55 mmHg, Po₂ 143 mmHg and B.E. 1.6 mmol/l, at Fio₂ 0.33 with a respiratory minute volume 6 l/min. One thousand milligrams of methyl-prednisolone and 20 mg of diphenhydramine chloride were administered instantly and manual ventilation with 100% oxygen was started.

Although 20 mg of ephedrine were twice administered in an attempt at management of persistent hypotension, the blood pressure failed to rise, as expected, with systolic pressure at 80 mmHg. Therefore, continuous administration of dopamine and dobutamine was started at a rate of 5 µg/kg/min alternately until the blood pressure returned normal.

Thirty minutes after the appearance of anaphylactoid symptoms, the correct placement

Department of Anesthesiology, Shimane Medical University, Izumo, Japan

Address reprint requests to Dr. Koh: Department of Anesthesiology, Shimane Medical University, 89-1 Enya-cho, Izumo, 693 Japan

of the Carlens' tube and Swan-Ganz catheter was confirmed by chest radiography in the operating room. No abnormal finding was seen in the radiography. At this time, procrastination of operation was declared by the anesthesiologist.

Approximately one hour after the initial administration of pancuronium, the blood pressure and heart rate stabilized at 140/70 mmHg and 100 beats/min respectively, when generalized skin flushing began to vanish. The arterial blood gas showed pH 7.205, P_{CO_2} 67 mmHg, P_{O_2} 495 mmHg and B.E. -3.2 mmol/l ($F_{IO_2} = 1.0$), when the patient was awake with a spontaneous breathing effort. Although arterial blood gas analysis revealed hypercarbia and slight metabolic acidosis, discontinuation of catecholamine administration seemed to be safe. To reverse the muscle relaxant effect, 1.5 mg of neostigmine with 0.5 mg of atropine were then administered. The tracheal tube was removed after confirmation of sufficient ventilation by the anesthesiologist. The patient was then carried into the recovery room.

In the recovery room, he was fully awake with spontaneous ventilation. Skin test of the forearm was carried out with 0.1 ml of diluted pancuronium (1/10) with control test using normal saline. Within minutes, a flare with erythema, 10 × 12 mm in diameter, developed without a wheal formation. It was impossible to distinguish the sensitivity of pancuronium from that of saline. Chest radiography in the recovery room also indicated no abnormal finding.

Seven days later, the patient was subjected to radical operation of esophageal cancer. The same premedication as used previously was followed by general and epidural anesthesia. After catheterization into the epidural space, anesthesia was induced with the same anesthetics as used previously, namely, thiamylal, SCC and fentanyl. Anesthesia was maintained by halothane, nitrous oxide and oxygen, and supplemented by mepivacaine into the epidural space. Muscle relaxation during operation was achieved by continuous administration of SCC at a rate of 5 mg/kg/hr. Operation was completed uneventfully.

Discussion

It has been claimed that pancuronium, an antidepolarizing muscle relaxant of the steroid structure, causes no histamine release. Because of this property, pancuronium is often used in asthmatic patients. However, it does not seem to be totally free from such action. Anaphylactoid reactions to this drug has been documented in six cases¹⁻⁶ (table 1). Case 5 was believed to be type 1 immunity-mediated hypersensitivity (anaphylaxis) and five others^{1-4,6} were defined as anaphylactoid reactions. However, no conclusive theory has been formulated as to the mechanism involved in these reactions.

The symptoms manifested in our case were considered to be defined as anaphylactoid reactions to pancuronium, in consideration of the following findings.

- (1) The patient had experienced no drug allergy.
- (2) The administration of pancuronium was followed within a few minutes by clinical symptoms such as hypotension, tachycardia and generalized skin flushing, even though pancuronium was administered at least 10 minutes after the administration of thiamylal, SCC and fentanyl.
- (3) Chest radiography never revealed such abnormal findings as pneumothorax, atelectasis, etc. that are caused by catheterization.
- (4) The same drugs except pancuronium were used in the operation but the operation was accomplished uneventfully.

The result of our skin test without a wheal formation was inconclusive. Skin test for anaphylactoid reactions to anesthetic drugs has been reported to produce a positive result in 70% of cases of anaphylactoid reactions⁷. However, the usefulness and reliability of skin test for confirmation of allergy remain controversial. The symptoms were managed by the administration of antihistamines, diphenhydramine and steroid. These might have affected the flare formation in our skin test, because the test was carried out approximately three hours after the administration of these drugs. Immunologic tests including lymphocyte transformation test, basophil degra-

Table 1. Anaphylactoid reactions due to pancuronium: case reports

No	Reference	Age	Sex	Previous exposure	History of Asthma	Symptoms	Skin test
1.	Heath (1973)	47	M	No	Yes	Bronchospasms	(+)
2.	Clark (1973)	48	F	No	No	Bronchospasms	(+)
3.	Buckland (1973)	42	F	No	Yes	Bronchospasms Hypotension	(+)
4.	Tweedie (1974)	58	M	No	No	Bronchospasms	(+)
5.	Brauer (1978)	57	M	Yes	No	Bronchospasms Cardiovascular collapse Pulmonary edema	(+)
6.	Mishima (1984)	47	M	No	No	Cardiovascular collapse	(+)
7	Koh (1986)	65	M	No	No	Cardiovascular collapse	(±)

nulation test and P-K test were desirable⁸. However, postoperatively the patient failed to regain a good general condition and died seven months after the operation. It was, therefore, impossible to obtain any conclusive evidence of anaphylactoid reactions in this patient.

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